OR-20

SYNTHESIS AND STRUCTURE-ACTIVITY RELATIONSHIPS OF THE NOVEL ISOTHIOBARBAMINE ANALOGUES WITH LOWERED BASICITY

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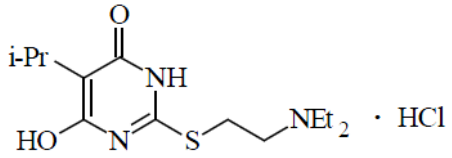
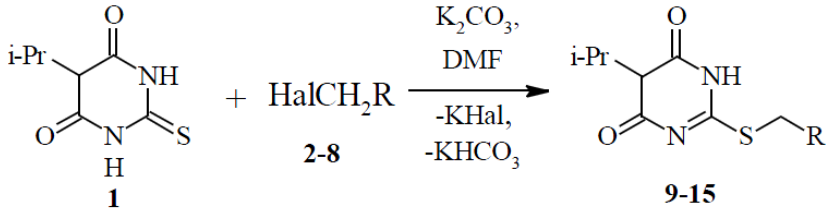
Isothiobarbamine is a synthetic adaptogen, derived from 6-hydroxy-5-isopropyl-2-thiouracil:

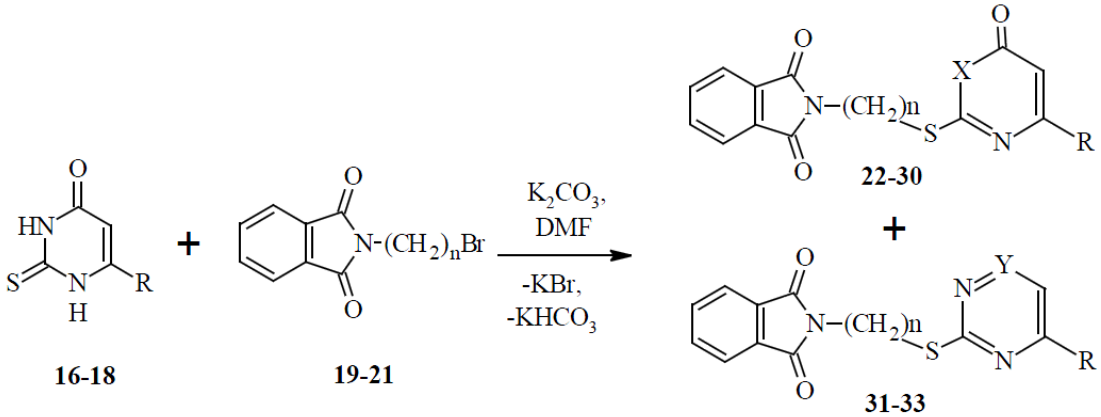


It was first described by Ukrainian scientists and showed a remarkable profile of biological activity in different *in vivo* tests, combined with low acute toxicity. Taking into consideration the results of L. Monti and G. Franchi on the structure-activity relationships of 5-(aminomethyl)-2-thiouracil derivatives *versus* the corresponding 5-(amidomethyl)-counterparts, we designed and prepared a series of different Isothiobarbamine analogues with lowered basicity, carrying an amido-function instead of diethylaminogroup, together with various substituents of the pyrimidin-4(3*H*)-one fragment:



1 **2-8** **9-15**

R = PhthN(**2,9**), PhthNCH$_2$(**3,10**), PhthN(CH$_2$)$_2$(**4,11**), Hal = Br.
R = C(O)NEt$_2$(**5,12**), C(O)N(CH$_2$)$_4$(**6,13**), C(O)N(CH$_2$)$_5$(**7**,**14**), C(O)N(CH$_2$CH$_2$)$_2$O(**8, 15**), Hal = Cl.



16-18 **19-21** **22-30** **31-33**

Где: R=NH$_2$, n=2(**22**),3(**23**), X=NH;
R=Me, n=1(**24**), 2(**25**), 3(**26**), X=NH; n=2(**31**),3(**32**), Y=CO(CH$_2$)$_n$NPhth;
R=CF$_3$, n=1(**27**), 2(**28**), 3(**29**), X=NH; n=2(**30**), X=N(CH$_2$)$_2$NPhth; n=2(**33**), Y=CO(CH$_2$)$_2$NPhth.
The latter derivatives showed some anti-HIV-1/2 activity, together with low toxicity in cellular assays.

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